REMARKS

Status of the claims

Claims 1-59 are pending in the application. Claims 20-33 stand rejected in the application. Claim 20 is amended currently. Claims 1-19 and 34-59 are withdrawn from consideration. No new matter is added.

Amendments to the claims

Claim 20 has been amended to overcome the 35 U.S.C. §103 rejection.

Claim rejection under 35 USC §103

Claims 20-33 stand rejected under 35 USC §103(a), as being unpatentable over **Larsen** et al. (U.S. Patent No. 6,592,843) in view of **Scheinberg** et al. (U.S. Patent No. 6,683,162) and **Wartchow** et al. (US2003/0082103 A1). Applicants respectfully traverse this rejection.

In the prior Office Action mailed July 17, 2008, the Examiner states that **Larsen** et al. disclose the encapsulation of radionuclides that emit alpha particles, such as Pb-212, Ac-225 into a liposome to generate a radionuclide-liposome conjugator system with PEG-affinic groups (page 3). Additionally, the Examiner states that the instant claims do not exclude an ionophore to actively transport the radionuclide across the lipid bilayer.

The Examiner also states that **Wartchow** et al. teach liposomes (bilayer or multilamellar vesicles) that may have the therapeutic agent/radionuclide-chelator complexes encapsulated within or trapped in the core of the liposomes. As such, the encapsulation of a radionuclide-conjugator complex within the multilamellar vesicles of **Wartchow** et al. provides for the limitation of a radiolabeled small liposome contained within a large liposome as the multilamellar vesicles have an onion-like form. Thus, the Examiner concludes, the references of **Larsen** et al. and **Wartchow** et al. are drawn to radionuclide-chelator liposomal conjugator systems and therefore it would be obvious with reasonable expectation for success for one skilled in the art to prepare a radionuclide-conjugator complex containing liposomes of **Larsen** et al. which may be multilamellar and contains a radiolabeled small liposome within a large liposome (pages 3-4).

Further, the Examiner states that **Scheinberg** et al. teach that radionuclide-chelator complexes may be attached to targeting entities (i.e. antibodies such as HERCEPTIN®) (page 5). As a result, the Examiner asserts that the radionuclide-chelator complexes of Larsen et al. (encapsulated within a liposome) may be attached to an antibody for site-specific targeting.

The Applicants respectfully submit that **Larsen** et al. disclose preparation of the liposomes using an active incorporation of radionuclides via ionophores (para 13 of Description). Claim 20 is amended to include the limitation that the liposomes of the instant invention are prepared by passive incorporation of the radionuclides.

Applicants respectfully submit that are several factors that illustrate the nonobviousness of the pending claims over the prior art. First, a person having ordinary skill in this art would not readily recognize, based on the prior relating to active entrapment, that passive entrapment could be utilized to reduce systemic release of radioactive decay intermediates by passively entrapping a radionuclide within small liposomal vesicles and then incorporating the entrapped radionuclide into the aqueous phase of large liposomes. Active entrapment requires an additional step of incorporating certain membrane molecules such as ionophores which may bind to select ions and facilitate its crossing across a membrane. There are also technical_challenges to the utilization of passive entrapment which render the instant invention nonobvious. For instance, passive entrapment of radionuclides may be deemed impractical by person of ordinary skill in the art because the incorporation rate is quite low and the need to remove any non-entrapped radionuclides.

The Applicants also submit that **Wartchow** et al. do not disclose larger liposomes having a diameter of about 600-1000nm. Therefore, the Applicants submit that the combined references would not enable a person of ordinary skill in the art to prepare liposomes of a size useful to reduce systemic release of radioactive decay intermediates.

Furthermore, the Applicants submit that the instant invention recites targeting agents (such as antibodies) on the outer surface of PEG-lipid structure. Neither **Scheinberg** et al. nor any combination of the references suggest the attachment of antibodies directly onto the PEG-lipid surface.

For a 35 U.S.C. §103 rejection to be valid, the combined references must at the very least suggest each and every element of the instant invention. None of the references disclose or suggest passive incorporation of radionuclides. None of the references disclose or suggest larger liposomes having a diameter of about 600-1000nm. None of the references disclose or suggest the attachment of antibodies directly onto the PEG-lipid surface. Accordingly, in view of the arguments presented herein, the Applicants respectfully request that the rejection of claims 20-33 under 35 U.S.C. §103(a) be withdrawn.

This is intended to be a complete response to the Office Action, mailed July 17, 2008. If any issues remain outstanding, the Examiner is respectfully requested to telephone the undersigned attorney of record for immediate resolution.

Respectfully submitted,

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